nism. Even after recovery from the respiratory tract infection, the patient found that he could still induce bradycardia and brief periods of cardiac arrest almost at will.

### DISCUSSION

It was felt that the clubbing of the fingers noted in this patient was familial, since it was present also in his son, who was healthy. The underlying cardiac change is believed to be well compensated rheumatic heart disease with aortic valvulitis. The bradycardia and cardiac arrest are probably manifestations of exaggerated vagotonia, induced through some mechanism which, although under voluntary control, is not known to the patient himself. Careful observation did not reveal any breath-holding or Valsalva maneuver in connection with the cessation of heartbeat. Apparently the patient simply abolished all sympathetic tone by complete mental and physical relaxation.

### SUMMARY

A case is presented of a patient with old rheumatic heart disease, who is able to produce cessation of heartbeat, apparently by volition alone.

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## Acute Renal Failure Manifesting as Water- And Salt-Losing Insufficiency

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CLINICAL SYNDROMES involving primary inability by the renal tubules to retain sodium have reached their fullest expression under the generic term "salt-losing nephritis." The condition usually is chronic, requiring long-term salt replacement therapy. Except for the reversible urinary salt loss of the diuretic phase of lower nephron nephrosis and that caused by diuretic agents, relatively little has been written of transient primary renal salt-losing syndromes. Following is a report of a case of reversible acute salt-losing renal insufficiency occurring after nephrectomy.

### REPORT OF A CASE

A 75-year-old white woman was admitted to the Highland-Alameda County Hospital on January 22, 1958, following a fall at home, after which she apparently lay on the floor all night, without voiding or eating, until found by a friend the next morning. She said that she had had no previous weakness, dizziness or imbalance and she was proud of being active. The last time she had needed the services of a physician was some forty years before for the birth of a child.

Upon examination it was noted that she was alert and spry-appearing. There was a small laceration on her forehead. The blood pressure was 104/60 mm. of mercury and the pulse rate 76 with a regular rhythm. The bladder was palpably enlarged above the pubis, and on catheterization 200 cc. of grossly bloody urine was removed.

There was motor weakness of the upper and lower extremities and assistance in walking was required. No neurological abnormalities were noted. X-ray films of the skull and chest taken at the time of admission were normal. The patient was then referred to the urological department where cystoscopy revealed the presence of what appeared to be diffuse, severe, acute hemorrhagic cystitis.

Submitted September 5, 1958.

In light of the patient's debility, an indwelling catheter was placed and laboratory examinations were obtained the next day. Results of centrifuged urine examination showed alkaline reaction, 2 plus albumin, no sugar, 140 leukocytes and 350 plus erythrocytes per high power field. Hemoglobin was 13 gm. per 100 cc. of blood, and leukocytes numbered 15,800 per cu. mm. Blood urea nitrogen was 100 mg. per 100 cc. and blood creatinine was 1.7 mg. per 100 cc. A urine culture grew an antibiotic resistant Aerobacter aerogenes. Phenolsulfonphthalein excretion was 5 per cent in the first hour and 35 per cent in the second hour.

The clinical impression was that the patient had acute and chronic hemorrhagic cystitis superimposed on probable carcinoma of the bladder with bilateral hydroureter. However, less than a month later, following rehydration, the blood urea nitrogen was down to 11 mg. per 100 cc. The hemoglobin content eventually became stable at 8.8 gm. per 100 cc.

An electrocardiogram and an x-ray film of the chest were interpreted as being within normal limits. Intravenous pyelograms obtained at this time revealed the presence of mild bilateral pyelectasis and caliectasis with a strong suspicion of a filling defect in the right renal pelvis. A cystoretrograde study carried out February 25, 1958, showed considerable resolution of the previously noted inflammatory process in the bladder, and there was no evidence of carcinoma. In differential phenolsulfonphthalein studies of the kidneys, there was excretion of 1 per cent of the dye from the right side and of 10 per cent from the left in 12 minutes. Bilateral pyelograms showed a ragged, irregular filling defect involving the right renal pelvis and associated caliectasia. Inflammatory changes involving the left upper ureter were also noted. Microscopic examination on culture of specimens of urine collected in a 24-hour period were negative for acid-fast organisms. A retrograde study a few days later again showed the irregularity of the right renal pelvis, consistent with the impression of right renal pelvis

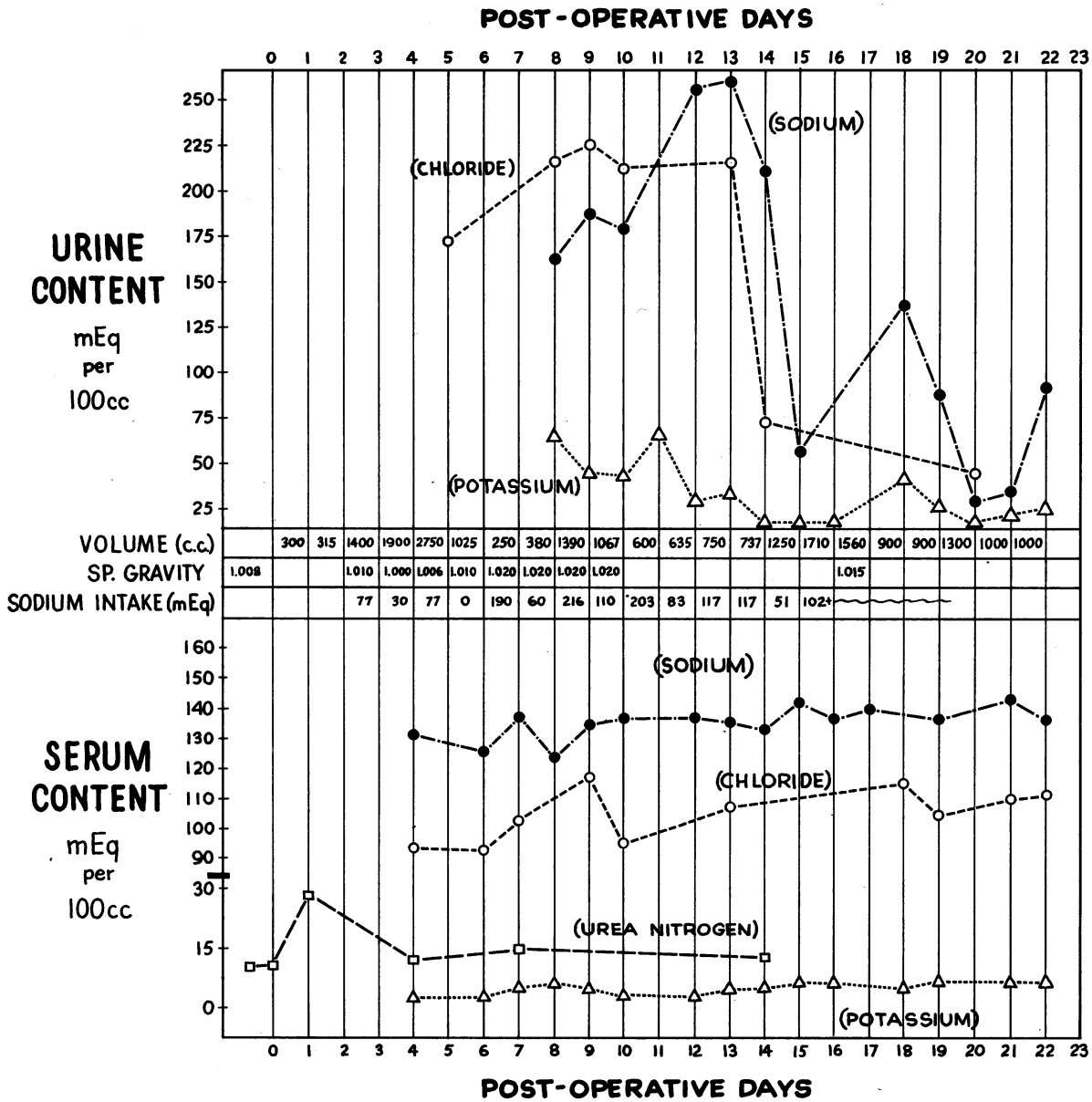


Chart 1.—Electrolyte contents of urine and serum, determined daily.

carcinoma. Another phenolsulfonphthalein determination on March 7, 1958, showed 47 per cent excretion in one hour and 15 per cent in the second hour. At her request the patient was discharged from the hospital, to return April 18. At the time of readmittance the blood urea nitrogen was 10 mg. per 100 cc. and the hemoglobin content 10.4 gm. per 100 cc. The specific gravity of the urine was 1.008 and the reaction alkaline.

On April 24, right transperitoneal morcellation nephrectomy was done with the patient under pentothal and nitrous oxide general anesthesia. The procedure was long and arduous owing to severe peripelvic inflammatory adherence to the vena cava and duodenum. The latter structure, which was intimately associated with both walls of the renal pelvis, had caused the pyelographic deformity. Separate closure was required for it.

Fluid replacement consisted of 2500 cc. of whole blood (1000 cc. of it given rapidly during a short period of acute hypotension) and 500 cc. of dextran. In the recovery room immediately after operation, it was noted that the blood pressure, which had been 110/60 mm. of mercury before operation, had risen to 180/110. In addition, there was peripheral cyanosis and a sustained clonus involving the right upper and lower extremities. It was thought that the acute surgical hypotension might have led to a cerebrovascular accident or that the amount of blood given had been excessive, causing an acute hy-

pertensive encephalopathic change. An immediate packed cell volume determination showed it to be 45 per cent, and it remained at that concentration for several days, implying that the distressing condition of the patient immediately after operaton was owing at least in part to hypervolemia.

The excised specimen, the pathologist reported, showed severe active and chronic ascending pyelonephritis and peripelvic inflammation.

The day after operation the blood pressure was within normal range and the patient was feeling well. During the night, oxygen inhalation therapy had been carried out and 2.0 gm. of albumin had been infused intravenously. Within 72 hours the patient was walking and taking fluids orally. The urinary volume rose from 315 cc. the first postoperative day to 2,790 cc. on the fourth day although the maximum daily fluid intake was only 1,500 to 2,000 cc. Specific gravity of the urine at this time ranged from 1.000 to 1.010. In the evening of the fourth postoperative day, the patient became restless and confused. It appeared that these phenomena might be ascribed to water intoxication. Since sodium determinations showed a moderately low content (Chart 1) hypertonic saline solution was given parenterally and the intake of fluids by mouth was restricted. Urinary electrolyte determinations were carried out daily and it became immediately apparent that the kidney was unable to retain salt. As the chart shows, serum sodium determination showed a moderately low content on the fourth postoperative day. During the next nine days the patient required increased amounts of sodium, up to 216 mg. per day in the form of hypertonic saline solution and molar lactate plus adequate potassium supplementation. The blood serum sodium levels, however, remained slightly low to normal, whereas the sodium content of the urine ranged upward from 157 mEq. per liter. Partial restriction of salt intake for one day resulted in a lowering of serum sodium, in edema formation and an increase in body weight. The blood urea nitrogen remained within normal limits, and serum creatinine on May 3 was 0.7 mg. per 100 cc. Carbon dioxide combining power was 26 mEq. per liter. An adrenocorticosteroid test in which 10 mg. of cortisone acetate was given intramuscularly during a 24-hour period of sodium chloride infusion at a constant rate, showed no response. An antidiuretic hormone vasopressin test on May 7 was inconclusive because of scant urinary output. On May 9, the 15th postoperative day, there was an abrupt decrease in urinary excretion of sodium, chloride and potassium, and thereafter the excretion of these chemicals remained within normal limits (except for one day when an increase was caused iatrogenically). An adrenocorticosteroid test was carried out again on May 14, and again gave no evidence that corticosteroid insufficiency was a factor in the salt-losing phenomenon in this case.

On May 19, 1958, the patient was discharged from the hospital. Subsequently observed twice, she was feeling well and had gained seven pounds in body weight.

## DISCUSSION

This case would appear to illustrate vividly the functional dichotomy that can exist between the various portions of the nephron. Most certainly it helps in the recognition of different selective forms of acute renal insufficiency in response to a gross insult to the entire organ. Well appreciated are the chronic renal-losing syndromes wherein given solutes are not reabsorbed and are lost individually and even collectively as sodium, chloride, potassium, amino acids, glucose, etc.[2,4,5,8] In this situation, specific tubular lesions have either altered the carbonic anhydrase system as a result of underlying pyelonephritis or there are lesions as yet indeterminate. Less frequently seen are segmental nephron disturbances, clinically and chemically discernible, occurring during the course of acute renal failure. Usually the two main categories of acute renal failure—renal ischemia and direct nephrotoxic renal tubular cell poisoning—have produced these effects on the nephron so rapidly and completely that sequential analysis of their effects is impossible. This results in what is seen in the classical case of acute renal failure—oliguria, isothenuria and retention of sodium, chloride, potassium and nitrogenous wastes. These lesions may give rise to transient, barely perceptible clinical conditions, or they may cause a complete irreversible renal cortical necrosis incompatible with life, the degree depending upon the severity of tubular necrosis.

The etiological consideration in this case would appear to be one of ischemia secondary to decreased supply of blood to the kidneys. Acute transient surgical hypotension is a well known cause of acute renal failure, particularly if prolonged and if renal disease already is present. It would appear from the laboratory findings that impaired renal function existed in this case. Of additional and possibly primary importance was hypervolemia caused by infusion of too much blood. One can only conjecture that renal erythemia may have brought about stasis and thrombosis of the arterioles supplying the tubular portion of the nephron. Even more speculative is what collective effect the hypotension, hypervolemic hypertension and related hypoxia may have had on the cerebrum.

The polyuria which occurred during the first four postoperative days would at first seem to be related to the apparent operative over-hydration. However, Perlmutter[10] emphasized the occasional case of acute renal failure with oliguria for a period or not present at all, then almost immediate entry into the diuretic phase. It is during this phase of polyuria that concommitant large amounts of sodium can be lost in the urine. In the present case, however, after only four days of polyuria there was a decided decrease in urinary output to between 300 and 1,000 cc. a day. That this period of increased water output was related to an initial phase of unresponsive renal tubules could be seen in the inability to concentrate the glomerular filtrate until the sixth postoperative day. Other investigators also have noted

occasional cases of acute renal failure in which deviation from specific gravity of 1.010 has occurred.[6,10,12]

Urinary excretion of salt in the present case continued despite curtailment of intake of both salt and fluid and the diagnostic use of adrenocorticosteroids. The abrupt cessation of salt loss after two weeks was undoubtedly related to the functional restoration and regeneration of the involved tubular cells. Unfortunately, since laboratory determinations for titratable acid and ammonia were not available, further elucidation of this mechanism was prevented. The urine reaction, however, was acid on the three occasions this factor was determined. This observation, coupled with one determination of a normal carbon dioxide combining power, would make it seem that the carbonic anhydrase and ammonia production buffer mechanisms were operative.

Without the therapist's knowledge of the coincidental cessation of hypernaturia, an oral supplementary program of 6 gm. of salt a day was instituted. That the tubular salt resorbtion function had by then been restored became acutely apparent when serum sodium determination 72 hours later showed a content of 163 mg. per 100 cc. The onset of edema was noted at that time. Indirect evidence that the anatomic integrity of the tubular cells and basement membrane were maintained can be seen in the blood urea nitrogen content: After the rise to 29 mg. per 100 cc. on the first postoperative day, it did not exceed 15 mg. per 100 ml. at any of many times determined.

The initial diagnostic complexity of what appeared to be a pure form of salt-losing nephritis made adrenal cortical and posterior pituitary hormonal studies mandatory. From the first reported cases by Thorn, Koepf and Clinton[13] in 1944 stemmed general recognition of the syndrome that they called "salt-losing nephritis." It was characterized by the systemic symptoms of a chronic urinary salt loss—loss of weight, asthenia and hypotension progressing to edema hypertension, nitrogen retention and cardiac failure. In pathological examination of the kidneys in a number of subsequent cases, no specific tubular changes were noted, but in almost all the changes of chronic pyelonephritis were observed.[3,7] It was found that the symptoms and the rate of progression of the intrinsic renal disease could be greatly decreased by giving supplementary sodium chloride and sodium bicarbonate. Of critical importance was the observation that despite the decided clinical resemblance to a deficiency of adrenal cortical hormone, the condition was refractory to these substances and was related to a primary renal tubular disorder. Hence the desoxycorticosterone acetate test for differentiation.

In the present case it was difficult to rule out a type of acute transient cerebral salt-wasting syndrome that is known to be associated with severe hypertension occurring with cerebral neoplasms, infections, severe encephalomalacia and trauma.[1,11,14] However, rarely in that condition is the condition abruptly self-limited as it was in the present case.


## SUMMARY

A case of an acute postoperative reversible water-losing and then salt-losing renal insufficiency is presented. It appeared to be owing to a phasic specific defect of the renal tubule cells that at first prevented the reabsorption of water and later the reabsorption of sodium and chloride.



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